L5 10640 COEXPRESS[redacted]

=> s l4 and l5

L6 8 L4 AND L5

=> dup rem l6

PROCESSING COMPLETED FOR L6
L7 7 DUP REM L6 (1 DUPLICATE REMOVED)

=> d ibib abs 1-7

L7 ANSWER 1 OF 7 MEDLINE
ACCESSION NUMBER: 96360044 MEDLINE
DOCUMENT NUMBER: 96360044
TITLE: Cloning and characterization of the human **GABAA receptor** alpha 4 subunit: identification of a unique diazepam-insensitive binding site.
AUTHOR: Yang W; Drewe J A; Lan N C
CORPORATE SOURCE: CoCensys, Inc., Iruine, CA 92718, USA.
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, **(1995 Nov 30)** 291 (3) 319-25.
Journal code: EN6. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612

AB Benzodiazepines modulate gamma-aminobutyric acid (GABA)-evoked chloride currents through a specific binding site at the **GABAA receptor**-chloride channel complex. The **heterogeneity** of diazepam-sensitive benzodiazepine binding sites (type I and type II) has been identified by pharmacological approaches both with native receptors and recombinant receptors coexpressing alpha, beta and gamma subunits. In addition, two distinguishable diazepam-insensitive benzodiazepine sites are found, spatially distributed between cerebral cortical and cerebellar regions. **Coexpression** of alpha 6 with beta 2 and gamma 2L subunits creates a pharmacologically similar benzodiazepine receptor to the diazepam-insensitive site observed in cerebellum, however, there is no evidence regarding the possible subunit combination forming the DI site in cerebral tissues. Here we report the cloning of the human alpha 4 cDNA and its pharmacology by **coexpression** of this alpha 4 subunit with beta 2 and gamma 2L subunits. This recombinant receptor complex showed a high affinity for the previously described benzodiazepine partial agonist bretazenill, the pyrazoloquinoline compounds CGS-9895 and CGS-9896, as well as the inverse agonists DMCM (methyl 6,7-dimethoxy 4-ethyl-beta-carboline-3-carboxylate) and Ro15-4513 as determined by [3H]Ro15-4513 binding. However, it is insensitive to the benzodiazepine type I selective compounds CL218.872 (3-methyl-6-[3-(trifluoromethyl)[phenyl]-1,2,4-triazolo[4.3-b]pyridazine) and zolpidem as well as the benzodiazepine full agonists diazepam, halazolam and midazolam. In addition, the benzodiazepine receptor ligands DMCM, beta-CCE (beta-carboline-3-carboxylate ethyl ester), Beta-CCM (beta-carboline-3-carboxylate methyl ester), FG-7142, CGS-9895 and CGS-9896 showed 7 to 10 times higher affinity for alpha 4 beta 2 gamma 2L. The pharmacology of the alpha 4 beta 2 gamma 2L receptor complex appears to resemble those of the diazepam-insensitive site found in the cerebral cortex. Our study thus suggests that this subpopulation of diazepam-insensitive GABAA receptors may be composed of alpha 4 beta 2 gamma 2L subunits.

L7 ANSWER 2 OF 7 MEDLINE
ACCESSION NUMBER: 95097362 MEDLINE

DOCUMENT NUMBER: 9509[illegible]2
TITLE: Four [illegible]ino acid exchanges convert a d[illegible]epam-insensitive, inverse agonist-preferring **GABAA receptor** into a diazepam-preferring **GABAA receptor** .
AUTHOR: Wieland H A; Luddens H
CORPORATE SOURCE: Laboratory for Molecular Neuroendocrinology, Center for Molecular Biology, Heidelberg, Germany..
SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, **(1994 Dec 23)** 37 (26) 4576-80.
Journal code: JOF. ISSN: 0022-2623.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199503

AB Benzodiazepines (BZ) exert their effects through GABAA receptors, which belong to the superfamily of ligand-gated ion channels. **Coexpression** of recombinant alpha, beta, and gamma subunits in a cell culture system mimics the BZ binding sites. The alpha variants largely determine the nature of the BZ binding site in such alpha i beta j gamma k **heteromultimers** (i = 1-6; j = 1-3; k = 1-3). Notably, the alpha 1 and alpha 6 variants confer high and low affinity for BZ agonists to the resulting receptor subtype, respectively. Glycine/glutamate and histidine/arginine positions in the alpha subunits of alpha x beta 2 gamma 2 receptors are involved in BZ I versus BZ II type selectivity. We now identify four amino acids in alpha 6 which together increase the affinity of the mutant alpha x beta 2 gamma 2 receptor for classical BZ receptor agonists above the level seen for any wild-type GABAA/BZ receptor. The most pronounced effect was due to an isoleucine to valine exchange. It simultaneously decreased the affinity for the BZ partial inverse agonist Ro 15-4513 20-fold and increased the affinity for diazepam 4-fold. The four amino acid residues stretch over most part of the N-terminal extracellular domain of the alpha subunit, suggesting that amino acids distant in the primary sequence form the BZ binding pocket.

L7 ANSWER 3 OF 7 MEDLINE
ACCESSION NUMBER: 93217527 MEDLINE
DOCUMENT NUMBER: 93217527
TITLE: Assembly of **GABAA receptor** subunits: alpha 1 beta 1 and alpha 1 beta 1 gamma 2S subunits produce unique ion channels with dissimilar single-channel properties.
AUTHOR: Angelotti T P; Macdonald R L
CORPORATE SOURCE: Department of Pharmacology, University of Michigan Medical School, Ann Arbor 48109-1687..
CONTRACT NUMBER: P01 NS19163 (NINDS)
GM 07767-14 (NIGMS)
SOURCE: JOURNAL OF NEUROSCIENCE, **(1993 Apr)** 13 (4) 1429-40.
Journal code: JDF. ISSN: 0270-6474.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199307

AB Recent experimental evidence has led to the hypothesis that **GABAA receptor** channel (GABAR) **heterogeneity** or receptor channel subtypes may occur by differential assembly of a given set of subunits into various configurations. Alternatively, assembly of subunits into mature GABARs may arise from an ordered process to produce a preferred form of the receptor channel, as seen for nicotinic ACh receptors. In the preceding article, we demonstrated that transient expression of GABAR alpha 1 and beta 1 subunits in mouse L929 fibroblast cells produced two different types of GABARs, when coexpressed with and without the gamma 2S subunit. Not only did these GABARs differ in their

GABA and diazepam pharmacology, but initial single-channel recordings suggested that the two types of GABARs (alpha 1 beta 1 and alpha 1 beta 1 gamma 2S) had different conductance and gating properties. It also appeared that alpha 1 beta 1 gamma 2S GABARs were preferentially formed over alpha 1 beta 1 GABARs, but it was not completely shown if both forms of GABARs were produced when a cell expressed all three subunits. To characterize further the assembly process and determine the preferred form, if it existed, it was necessary to obtain a kinetic "fingerprint" for both alpha 1 beta 1 and alpha 1 beta 1 gamma 2S GABARs. Thus, single-channel patch-clamp recording and kinetic analysis of receptor channel gating were performed. For both alpha 1 beta 1 and alpha 1 beta 1 gamma 2S GABARs, GABA evoked single-channel openings to both a main conductance (15 and 29 pS, respectively) and a subconductance level (10 and 21 pS, respectively) with greater than 90% of the total current through the main conductance level openings. The two GABAR populations were further differentiated by their open and burst properties. On average, alpha 1 beta 1 gamma 2S GABARs opened for almost three times the duration as alpha 1 beta 1 GABARs (6.0 vs 2.3 msec, respectively) and had three openings per burst. alpha 1 beta 1 GABARs opened predominantly as single opening bursts. Using the conductance and gating properties to differentiate the two GABAR populations, we determined that alpha 1 beta 1
GABARs were rarely, if ever, formed upon **coexpression** of all three subunits, suggesting that alpha 1 beta 1 gamma 2S GABARs were the preferred final form of the receptor channel. Also, the homogeneity of the
conductance and gating properties of alpha 1 beta 1 gamma 2S GABARs among the different patches studied implied that a single preferred configuration of GABARs may exist.(ABSTRACT TRUNCATED AT 400 WORDS)

L7 ANSWER 4 OF 7 MEDLINE
ACCESSION NUMBER: 93341494 MEDLINE
DOCUMENT NUMBER: 93341494
TITLE: Regional gamma-aminobutyric acid sensitivity of t-butylbicyclophosphoro[35S]thionate binding depends on gamma-aminobutyric acidA receptor alpha subunit.
AUTHOR: Korpi E R; Luddens H
CORPORATE SOURCE: Laboratory of Molecular Neuroendocrinology, University of Heidelberg, Germany..
SOURCE: MOLECULAR PHARMACOLOGY, **(1993 Jul)** 44 (1) 87-92. Journal code: NGR. ISSN: 0026-895X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199311
AB gamma-Aminobutyric acid (GABA) modulates the convulsant binding site on GABAA receptors labeled by t-butylbicyclophosphoro[35S] thionate ([35S]TBPS). The modulation varies between different brain regions, reflecting the molecular **heterogeneity** of the GABAA receptors. In rat brain cryostat sections, the main sensitivity difference to GABA between brain regions was observed within the cerebellum. [35S]TBPS binding in the granule cell layer was more sensitive to GABA than was that
in the molecular layer and was detected only after blockade of the GABA agonist sites by the specific GABAA antagonists SR 95531, RU 5135, and bicuculline. This indicates that the [35S]TBPS binding sites in cerebellar
granule cells were blocked by endogenous GABA. In contrast, the internal rim of the granule cell layer had a small amount of binding that was largely insensitive to 50 microM GABA. The molecular basis for the sensitivity difference could be traced to the alpha subunits of the **GABAA receptor**. Expression in human embryonic kidney 293 cells of alpha 6 beta 2 gamma 2 receptors produced [35S] TBPS binding sites that were about 10-fold more sensitive to inhibition by GABA than were those inherent to alpha 1 beta 2 gamma 2 receptors. **Coexpression** of alpha 6 and beta 2 subunits produced [35S]TBPS binding sites that were largely insensitive to GABA inhibition, resembling

in their pharmacolo[redacted]al profile the sites in the in[redacted]nal granule cell layer. Furthermore, [redacted]e differences between alpha 6 [redacted]a 2 and alpha 6 beta 2 gamma 2 receptors stress the importance of the gamma 2 subunit for the proper pharmacological fingerprint of the rest of the granule cell layer. The neurosteroid 5 alpha-pregnan-3 alpha-ol-20-one affected the binding in both alpha 1 beta 2 gamma 2 and alpha 6 beta 2 gamma 2 receptors, but inhibition was greater in alpha 6-containing than in alpha 1-containing receptors, suggesting differential coupling of both GABA and neurosteroid sites with the convulsant site. These data might serve as a platform for additional studies to assess the amino acid residues in the two alpha subunits that are critically involved in the allosteric interactions between the GABAA agonist/antagonist or neurosteroid domains and the convulsant site.

L7 ANSWER 5 OF 7 MEDLINE
ACCESSION NUMBER: 89181956 MEDLINE
DOCUMENT NUMBER: 89181956
TITLE: Importance of a novel **GABAA receptor** subunit for benzodiazepine pharmacology.
AUTHOR: Pritchett D B; Sontheimer H; Shivers B D; Ymer S; Kettenmann H; Schofield P R; Seeburg P H
CORPORATE SOURCE: ZMBH, Universitat Heidelberg, FRG..
SOURCE: NATURE, **(1989 Apr 13)** 338 (6216) 582-5.
Journal code: NSC. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198907
AB Neurotransmission effected by GABA (gamma-aminobutyric acid) is predominantly mediated by a gated chloride channel intrinsic to the **GABAA receptor**. This **heterooligomeric** receptor exists in most inhibitory synapses in the vertebrate central nervous system (CNS) and can be regulated by clinically important compounds such as benzodiazepines and barbiturates. The primary structures of **GABAA receptor** alpha- and beta-subunits have been deduced from cloned complementary DNAs. Co-expression of these subunits in **heterologous** systems generates receptors which display much of the pharmacology of their neural counterparts, including potentiation by barbiturates. Conspicuously, however, they lack binding sites for, and consistent electrophysiological responses to, benzodiazepines. We now report the isolation of a cloned cDNA encoding a new **GABAA receptor** subunit, termed gamma 2, which shares approximately 40% sequence identity with alpha- and beta-subunits and whose messenger RNA is prominently localized in neuronal subpopulations throughout the CNS. Importantly, **coexpression** of the gamma 2 subunit with alpha 1 and beta 1 subunits produces GABAA receptors displaying high-affinity binding for central benzodiazepine receptor ligands.

L7 ANSWER 6 OF 7 MEDLINE
ACCESSION NUMBER: 90076482 MEDLINE
DOCUMENT NUMBER: 90076482
TITLE: Pharmacological characterization and region-specific expression in brain of the beta 2- and beta 3-subunits of the rat **GABAA receptor**.
AUTHOR: Lolait S J; O'Carroll A M; Kusano K; Mahan L C
CORPORATE SOURCE: Laboratory of Cell biology, NIMH, Bethesda, MD 20892..
SOURCE: FEBS LETTERS, **(1989 Nov 20)** 258 (1) 17-21.
Journal code: EUH. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199003
AB The cDNA for a third beta-subunit of the rat **GABAA receptor** has been cloned using another beta-subunit, which we had previously cloned [(1989) FEBS Lett. 246, 145-148], as a probe. The

approximately 8-kb [redacted]NA for this beta-subunit (terme[redacted]beta 2) encodes a protein of 474 amin[redacted]acid residues that shares appro[redacted]ately 80% sequence identity with the rat and bovine beta 1- and beta 3-subunits. **Coexpression** of the cloned beta-subunit cDNA with the alpha 1-subunit cDNA of the rat **GABAA receptor** in Xenopus oocytes produced a functional receptor and Cl- channel with pharmacological characteristics of a **GABAA receptor**. In contrast to interchanging alpha-subunits [(1988) Nature 335, 76-79], exchange of beta 2- or beta 3-subunits in an alpha 1/beta receptor complex did not markedly alter the pharmacological properties of expressed receptors. In situ hybridization histochemistry with synthetic subunit-specific oligo-deoxynucleotide probes revealed a region-specific expression of alpha 1-, beta 2- and beta 3-subunit mRNAs in the rat central nervous system. These observations provide an additional molecular basis for the functional **heterogeneity** in the **GABAA receptor** complex.

L7 ANSWER 7 OF 7 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 89058643 MEDLINE
DOCUMENT NUMBER: 89058643
TITLE: Transient expression shows ligand gating and allosteric potentiation of **GABAA receptor** subunits.
AUTHOR: Pritchett D B; Sontheimer H; Gorman C M; Kettenmann H; Seeburg P H; Schofield P R
CORPORATE SOURCE: Laboratory of Molecular Neuroendocrinology, ZMBH, University of Heidelberg, Federal Republic of Germany..
SOURCE: SCIENCE, **(1988 Dec 2)** 242 (4883) 1306-8. Journal code: UJ7. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198903
AB Human gamma-aminobutyric acid A (**GABAA**) **receptor** subunits were expressed transiently in cultured mammalian cells. This expression system allows the simultaneous characterization of ligand-gated ion channels by electrophysiology and by pharmacology. Thus, **coexpression** of the alpha and beta subunits of the **GABAA receptor** generated GABA-gated chloride channels and binding sites for **GABAA receptor** ligands. Channels consisting of only alpha or beta subunits could also be detected. These homomeric channels formed with reduced efficiencies compared to the **heteromeric** receptors. Both of these homomeric GABA-responsive channels were potentiated by barbiturate, indicating that sites for both ligand-gating and allosteric potentiation are present on receptors assembled from either subunit.

=> s gabab

L8 3037 GABAB

=> d his

(FILE 'HOME' ENTERED AT 16:10:24 ON 19 MAY 2000)

FILE 'MEDLINE, BIOSIS, BIOTECHNO' ENTERED AT 16:10:41 ON 19 MAY 2000
L1 9581 S GABA? RECEPTOR
L2 536512 S HETERO?
L3 571 S L1 AND L2
L4 415 S L3 AND PY <1998
L5 10640 S COEXPRESSION
L6 8 S L4 AND L5
L7 7 DUP REM L6 (1 DUPLICATE REMOVED)

L8 3037 S GABAB

=> s gabab?

L9 3068 GABAB?

=> s l9 and l2

L10 146 L9 AND L2

=> d ibib abs 140-146

L10 ANSWER 140 OF 146 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1990:334740 BIOSIS
DOCUMENT NUMBER: BA90:42759
TITLE: INHIBITION OF BACLOFEN BINDING TO RAT CEREBELLAR MEMBRANES BY PHACLOFEN SACLOFEN 3 AMINOPROPYLPHOSPHONIC ACID AND RELATED GABA-B RECEPTOR ANTAGONISTS.
AUTHOR(S): DREW C A; JOHNSTON G A R; KERR D I B; ONG J
CORPORATE SOURCE: DEP. PHARMACOL., UNIV. SYDNEY, SYDNEY, NSW 2006, AUST.
SOURCE: NEUROSCI LETT, (1990) 113 (1), 107-110.
CODEN: NELED5. ISSN: 0304-3940.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The inhibition of the binding of the **GABAB** agonist [3H](-)-baclofen to rat cerebellar membranes by some sulfonic and phosphonic acid analogue of GABA has been studied. These analogues have been shown to act a **GABAB** antagonists in the rate cortical wedge and the guinea-pig isolated ileum preparations. The order of potency of phaclofen (IC50 118 .mu.m), 2-hydroxysaclofen (IC50 5.1 .mu.M) and saclofen (IC50 7.8 .mu.M) as inhibitors of [3H](-)-baclofen binding was similar to the order of potency of these compounds as **GABAB** antagonists, whereas 3-aminopropylphophonic acid (IC50 1.5 .mu.M) and 4-aminobutyiphosphonic acid (IC50 3.9 .mu.M) were much more potent than anticipated from their relatively weak **GABAB** antagonist actions. These results indicate that inhibition of [3H](-)-baclofen binding to rat cerebellar membranes does not reflect antagonist activity at **GABAB** receptors seen in the rat cortical wedge preparation or the guinea-pig isolated ileum preparations. This may indicate a **heterogeneity** of **GABAB** binding and receptor sites.

L10 ANSWER 141 OF 146 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1990:267286 BIOSIS
DOCUMENT NUMBER: BA90:9372
TITLE: SUBTYPES OF GAMMA AMINOBUTYRIC ACID RECEPTORS EXPRESSED IN XENOPUS OOCYTES INJECTED WITH GUINEA-PIG CEREBRAL MESSENGER RNA.
AUTHOR(S): SEKIGUCHI M; OKAMOTO K; SAKAI Y
CORPORATE SOURCE: DEP. OF PHARMACOL., NATL. DEFENSE MED. COLL., TOKOROZAWA SAITAMA 359, JAPAN.
SOURCE: J NATL DEF MED COLL, (1989) 14 (4), 218-226.
CODEN: BIDZDQ. ISSN: 0385-1796.
FILE SEGMENT: BA; OLD
LANGUAGE: Japanese
AB For the purpose of investigating the subtypes of receptors for .gamma.-aminobutyric acid (GABA, a major inhibitory neurotransmitter in mammalian central nervous systems), the mRNA extracted from the guinea pig cerebrum was injected into Xenopus laevis oocytes, and expressed GABA receptors were electrophysiologically and pharmacologically studied using a voltage-clamp technique. As a result, it was found that two types of GABA receptors were expressed in Xenopus oocytes, one was the GABAA receptor which was sensitive to picrotoxinin (a chloride channel blocker) and insensitive to phaclofen (a specific antagonist of the **GABAB** receptor), and the other was the picrotoxinin-insensitive and phaclofen-sensitive **GABAB** receptor. Furthermore, it was also found that the responses of mRNA-injected oocytes to GABA were antagonized

by bicuculline (a competitive antagonist specific to the GABAA receptor) in some oocytes, where bicuculline functioned as a more potent agonist than GABA in other oocytes. This finding suggests that there is **heterogeneity** in the GABAA receptors expressed in Xenopus oocytes by injection of guinea pig cerebral mRNA.

L10 ANSWER 142 OF 146 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1990:158300 BIOSIS
DOCUMENT NUMBER: BA89:85718
TITLE: DIFFERING ACTIONS OF BACLOFEN AND 3 AMINOPROPYLPHOSPHINIC ACID IN RAT NEOCORTICAL SLICES.
AUTHOR(S): ONG J; KERR D I B; JOHNSTON G A R; HALL R G
CORPORATE SOURCE: DEP. ANAESTHESIA INTENSIVE CARE, UNIV. ADELAIDE, ADELAIDE, S.A. 5000, AUSTRALIA.
SOURCE: NEUROSCI LETT, (1990) 109 (1-2), 169-173.
CODEN: NELED5. ISSN: 0304-3940.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Rat neocortical slices maintained in Mg2+-free Krebs medium developed spontaneous paroxysmal discharges which were attenuated or suppressed by the .gamma.-aminobutyric acid-B (**GABAB**) receptor agonist baclofen, occasionally accompanied by a slight hyperpolarisation, and antagonised by the specific **GABAB**-receptor antagonist, 2-OH salcofen. Over the same dose range, the GABA-analogue 3-amino-propylphosphinic acid (3-APA) caused a marked, prompt hyperpolarisation with little or no effect on the frequency of the discharges, although their amplitude was attenuated. In the presence of 2-OH-saclofen, 3-APA still induced a hyperpolarisation but the amplitude of the discharges was no longer affected. This marked differences in action between baclofen and
3-APA in the rat neocortical slices suggests there may be a **heterogeneity** of **GABAB**-receptors.

L10 ANSWER 143 OF 146 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1989:97129 BIOSIS
DOCUMENT NUMBER: BA87:51265
TITLE: POSTSYNAPTIC POTENTIALS RECORDED IN NEURONS OF THE CAT'S LATERAL GENICULATE NUCLEUS FOLLOWING ELECTRICAL STIMULATION
OF THE OPTIC CHIASM.
AUTHOR(S): BLOOMFIELD S A; SHERMAN S M
CORPORATE SOURCE: DEP. OPHTHALMOL., NEW YORK UNIV. MED. CENT., 550 FIRST AVE,
NEW YORK, N.Y. 10016.
SOURCE: J NEUROPHYSIOL (BETHESDA), (1988) 60 (6), 1924-1945.
CODEN: JONEA4. ISSN: 0022-3077.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB We recorded intracellularly from X and Y cells of the cat's lateral geniculate nucleus and measured the postsynaptic potentials (PSPs) evoked from electrical stimulation of the optic chiasm. We used an in vivo preparation and computer averaged the PSPs to enhance their signal-to-noise ratio. The vast majority (46 of 50) of our sample of X and
Y cells responded to stimulation of the optic chiasm with an excitatory postsynaptic potential (EPSP) followed by an inhibitory postsynaptic potential (IPSP); these were tentatively identified as relay cells. We quantified several parameters of these PSPs, including amplitude, latency,
time to peak (i.e., rise time), and duration. Among the relay cells, the latencies of both the EPSP and action potential evoked by optic chiasm stimulation were shorter in Y cells than in X cells. Furthermore, the difference between the latencies of the EPSP and action potential was shorter for Y cells than for X cells. This means that the EPSPs generated in Y cells reached threshold for generation of action potentials faster than did those in X cells. The EPSPs of Y cells also displayed larger amplitudes and faster rise times than did those in X cells, but neither of
these distinctions was sufficient to explain the shorter latency

difference between [redacted] EPSP and action potential for cells. The EPSPs recorded in relay Y [redacted]ells had longer durations than those in relay X cells. Our data suggest that the subsequent IPSP actively terminates the EPSP, which, in turn, suggests that the time interval between EPSP and IPSP onsets is longer in Y cells than in X cells. Furthermore, we found that, for individual Y cells, the latency and duration of the evoked EPSP were inversely related. These observations lead to the conclusion that the latency of IPSPs activated from the optic chiasm is relatively constant among Y cells and thus independent of the EPSP latencies. Thus the excitation and inhibition produced in individual geniculate Y cells may originate from different populations of retinogeniculate axons. The IPSPs recorded in geniculate relay cells following optic chiasm stimulation could be divided into three groups based on their durations. The majority of both X and Y cells showed short-duration IPSPs, whereas the remainder of Y cells displayed medium-duration IPSPs, and the remaining X cells displayed long-duration IPSPs. A positive correlation was seen between the time to peak and duration of these IPSPs. The reversal potential of short duration IPSPs, for both X and Y cells, was about -76 mV. In contrast, the reversal potentials of both medium- and long-duration IPSPs were about -102 mV. These data suggest that, in response to optic chiasm stimulation, both X and Y cells display two types of inhibition that differ in their ionic conductances. We found no evidence that any of the relay cells produced amixed IPSP. Given prior evidence that .gamma.-aminobutyric acid (GABA) is the dominant inhibitory neurotransmitter in the lateral geniculate nucleus, we propose that short-duration IPSPs reflect a chloride conductance that may be mediated by a GAGAA receptor, whereas medium- and long-duration IPSPs may each reflect a potassium conductance mediated by **GABAB** receptors. We found that the standard deviations for 8 of 10 PSP parameters were greater for relay X cells than for relay Y cells. This finding extends to PSPs a previous assertion, based on other morphological and physiological data, that the C cell population is more **heterogeneous** than is the Y cell population. We recorded from four neurons, all X cells, that did not display any obvious IPSP following stimulation of the optic chiams. These cells could not be driven antidromically with electrical stimulation of the visual cortex. They have thus been tentatively identified as interneurons. In addition, the evoked EPSPs in these cells were roughly 10 times longer in duration than those generated in the relay cells. However, the other tested response properties of these neurons, which included an evaluation of their receptive field properties, were indistinguishable from those of relay X cells.

L10 ANSWER 144 OF 146 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1987:254345 BIOSIS
DOCUMENT NUMBER: BA84:7317
TITLE: GABA-A AND GABA-B RECEPTOR SITE DISTRIBUTION IN THE RAT CENTRAL NERVOUS SYSTEM.
AUTHOR(S): BOWERY N G; HUDSON A L; PRICE G W
CORPORATE SOURCE: MERCK SHARP AND DOHME RES. LAB., NEUROSCI. RES. CENT., TERLINGS PARK, EASTWICK RD., HARLOW, ESSEX CM20 2QR, UK.
SOURCE: NEUROSCIENCE, (1987) 20 (2), 365-384.
CODEN: NRSCDN. ISSN: 0306-4522.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB An autoradiographic procedure has been used to determine the quantitative distributions of .gamma.-aminobutyric acid (GABAA and **GABAB**) receptor subtypes in rat brain. Although the concentrations of both receptor binding sites were similar in some brain regions GABAA sites generally outnumbered **GABAB** sites. The highest concentration of GABAA sites were detected in the frontal cortex, the granule cell layer of the cerebellum, the olfactory bulb and the thalamic medial geniculate. The highest concentration of **GABAB** sites occurred in the molecular layer of the cerebellum, the interpeduncular nucleus, frontal cortex,

anterior olfactory [redacted]leus and thalamic nuclei. In a[redacted]tion the globus pallidus, temporal [redacted]rtex, lateral posterior thalamus[redacted] superior colliculus, pontine nucleus, raphe magnus, spinal trigeminal tract and substantia gelatinosa contained significantly more **GABAB** sites than GABAA sites. The physiological and pharmacological significance of this **heterogeneity** has yet to be determined.

L10 ANSWER 145 OF 146 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1986:164205 BIOSIS
DOCUMENT NUMBER: BA81:74621
TITLE: EVIDENCE FOR GAMMA AMINOBUTYRIC-ACID AUTORECEPTORS IN MEDIAN EMINENCE.
AUTHOR(S): ANDERSON R A; MITCHELL R
CORPORATE SOURCE: MRC BRAIN METABOLISM UNIT, DEP. PHARMACOL., 1 GEORGE SQUARE, EDINBURGH EH8 9JZ, SCOTLAND.
SOURCE: EUR J PHARMACOL, (1985) 118 (3), 355-358.
CODEN: EJPHAZ. ISSN: 0014-2999.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The effect of the selective **GABAB** receptor agonist baclofen was examined on stimulus-induced release of [3H]GABA from crude synaptosomal preparations of median eminence (ME) and pituitary neurointermediate lobe (NI). Baclofen stereospecifically inhibited release of [3H]GABA in a concentration-dependent manner from ME but had no effect in NI. The effect of (.+-.) baclofen was partly antagonized by the putative **GABAB** receptor antagonist .delta.-aminovaleric acid, but these experiments were complicated by a degree of **heteroexchange**. These results provide the first evidence for **GABAB** autoreceptors in the CNS.

L10 ANSWER 146 OF 146 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1986:111998 BIOSIS
DOCUMENT NUMBER: BA81:22414
TITLE: THE REGULATION OF NORADRENALINE SYNTHESIS IN CENTRAL NERVE TERMINALS BY AUTORECEPTORS AND **HETERORECEPTORS** IN RAT.
AUTHOR(S): BIRCH P J; FILLENZ M
CORPORATE SOURCE: UNIV. LAB. PHYSIOLOGY, PARKS ROAD, OXFORD OX1 3PT, U.K.
SOURCE: NEUROSCI LETT, (1985) 59 (2), 197-202.
CODEN: NELED5. ISSN: 0304-3940.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The effects of .alpha.2-adrenoceptor and .gamma.-aminobutyric acidB (**GABAB**) receptor activation on noradrenaline synthesis were measured in rat hippocampal synaptosomes. The results show that .alpha.2-autoreceptors and **GABAB heteroreceptors** inhibit K+-accelerated synthesis; they have no effect on basal synthesis.

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(FILE 'HOME' ENTERED AT 16:10:24 ON 19 MAY 2000)

FILE 'MEDLINE, BIOSIS, BIOTECHNO' ENTERED AT 16:10:41 ON 19 MAY 2000
L1 9581 S GABA? RECEPTOR
L2 536512 S HETERO?
L3 571 S L1 AND L2
L4 415 S L3 AND PY <1998
L5 10640 S COEXPRESSION
L6 8 S L4 AND L5
L7 7 DUP REM L6 (1 DUPLICATE REMOVED)
L8 3037 S GABAB
L9 3068 S GABAB?
L10 146 S L9 AND L2

=> s dimer or dimeric or heterodimer or heterodimeric

L11 75555 DIMER OR DIMERIC OR HETERODIMER OR HETERODIMERIC

=> s l11 and l9

L12 8 L11 AND L9

=> dup rem l12

PROCESSING COMPLETED FOR L12
L13 6 DUP REM L12 (2 DUPLICATES REMOVED)

=> d ibib abs 1-6

L13 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:109727 BIOSIS
DOCUMENT NUMBER: PREV200000109727
TITLE: gamma-Aminobutyric acidB receptors: First of the functional
metabotropic heterodimers.
AUTHOR(S): Bowery, Norman G. (1); Enna, S. J.
CORPORATE SOURCE: (1) Medical School, Department of Pharmacology, University of Birmingham, Edgbaston, Birmingham, B15 2TT UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (Jan., 2000) Vol. 292, No. 1, pp. 2-7.
ISSN: 0022-3565.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Activation of the metabotropic gamma-aminobutyric acidB (**GABAB**) receptor increases K+ conductance and decreases Ca2+ channel activity in neuronal membranes. Studies with a number of new **GABAB** receptor agonists and antagonists reveal that in addition to their muscle relaxant effects, agonists display analgesic activity and reduce the craving for cocaine. With regard to **GABAB** receptor antagonists, preclinical data suggest they improve cognitive performance and possess antidepressant and antiepileptic potential. With a high-affinity **GABAB** antagonist, the structural properties of the receptor were characterized through expression cloning. Moreover, it has been found that expression of a fully functional **GABAB** receptor requires coupling between two separate and distinct gene products: **GABAB** R1 and **GABAB** R2. Besides being the first example of a functional heterodiameric metabotropic receptor, the components and molecular configuration of the **GABAB** receptor suggest novel mechanisms for producing pharmacologically distinct subtypes of G protein-coupled receptors.

L13 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:482190 BIOSIS
DOCUMENT NUMBER: PREV199900482190
TITLE: gamma-aminobutyric acid type B receptor splice variant proteins GBR1a and GBR1b are both associated with GBR2 in situ and display differential regional and subcellular distribution.
AUTHOR(S): Benke, Dietmar (1); Honer, Michael; Michel, Claudia; Bettler, Bernhard; Mohler, Hanns
CORPORATE SOURCE: (1) Institute of Pharmacology, ETH and University of Zurich, Winterthurerstrasse 190, CH-8057, Zurich Switzerland
SOURCE: Journal of Biological Chemistry, (Sept. 17, 1999) Vol. 274,
No. 38, pp. 27323-27330.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The subunit architecture of gamma-aminobutyric acid, type B (**GABAB**), receptors in situ is largely unknown. The **GABAB** receptor variants, characterized by the constituents GBR1a and GBR1b, were

therefore analyzed with regard to their subunit composition as well as their regional and subcellular distribution in situ. The analysis was based on the use of antisera recognizing selectively GBR1a, GBR1b, and GBR2. Following their solubilization, GBR1a and GBR1b were both found by immunoprecipitation to occur as heterodimers associated with GBR2. Furthermore, monomers of GBR1a, GBR1b, or GBR2 were not detectable, suggesting that practically all **GABAB** receptors are heterodimers in situ. Finally, there was no evidence for an association of GBR1a with GBR1b indicating that these two constituents represent two different receptor populations. A size determination of solubilized **GABAB** receptors by sucrose density centrifugation revealed two distinct peaks of which one corresponded to **dimeric** receptors, and the higher molecular weight peak pointed to the presence of yet unknown receptor-associated proteins. The distribution and relative abundance of GBR2 immunoreactivity corresponded in all brain regions to that of the sum of GBR1a and GBR1b, supporting the view that most if not all GBR1 proteins are associated with GBR2. However, GBR1a was present preferentially at postsynaptic densities, whereas GBR1b may be mainly attributed to presynaptic or extrasynaptic sites. Thus, GBR1a and GBR1b are both associated with GBR2 to form heterodimers at mainly different subcellular locations where they are expected to subserve different functions.

L13 ANSWER 3 OF 6 MEDLINE
ACCESSION NUMBER: 1999459274 MEDLINE
DOCUMENT NUMBER: 99459274
TITLE: Heterodimerization of a functional **GABAB** receptor is mediated by parallel coiled-coil alpha-helices.
AUTHOR: Kammerer R A; Frank S; Schulthess T; Landwehr R; Lustig A; Engel J
CORPORATE SOURCE: Department of Biophysical Chemistry, Biozentrum, University of Basel, Switzerland.
SOURCE: BIOCHEMISTRY, (1999 Oct 5) 38 (40) 13263-9. Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY WEEK: 20000104
AB A detailed understanding of **GABAB** receptor assembly is an important issue in view of its role as attractive target for treatment of epilepsy, anxiety, depression, cognitive defects, and nociceptive disorders. Heteromerization of **GABAB**-R1 and **GABAB**-R2 subunits is a prerequisite for the formation of a functional **GABAB** receptor. Each individual subunit contains one stretch of approximately 30 amino acid residues within its intracellular C-terminal domain that mediates heteromer formation. To investigate the mechanism of the **GABAB**-R1/**GABAB**-R2 interaction and to assess the subunit stoichiometry of the complex, recombinant polypeptide chain fragments containing the heteromerization site were produced by heterologous gene expression in Escherichia coli. When mixed in equimolar amounts, these peptides preferentially formed parallel coiled-coil heterodimers under physiological buffer conditions. This demonstrates that the short C-terminal regions are sufficient to determine the specificity of interaction between **GABAB** receptor subunits. In contrast, isolated **GABAB**-R1 peptides folded into relatively unstable homodimers, whereas **GABAB**-R2 peptides were largely unstructured. Together with the data reported in the literature, the results presented here indicate that the functional **GABAB** receptor is a **heterodimer** assembled by parallel coiled-coil alpha-helices.

L13 ANSWER 4 OF 6 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000052363 MEDLINE
DOCUMENT NUMBER: 20052363

TITLE: Calc sensing properties of the GAB[redacted] receptor.
AUTHOR: Wise Green A; Main M J; Wilson R; [redacted]ser N; Marshall F H
CORPORATE SOURCE: Receptor Systems, Molecular Pharmacology Unit, Glaxo Wellcome Medicines Research Centre, Stevenage, Hertfordshire, UK.
SOURCE: NEUROPHARMACOLOGY, (1999 Nov) 38 (11) 1647-56.
Journal code: NZB. ISSN: 0028-3908.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY WEEK: 20000204
AB The GABA(B) receptor has been shown to consist of a **heterodimer** of two related 7-transmembrane receptors **GABAB**-R1 and GABA(B)-R2. These receptors share close homology to the Ca2+-sensing receptor and also to the metabotropic glutamate receptors, which have also been shown to respond to extracellular calcium. We show here that the GABA(B) receptor also has Ca2+ sensing properties. Ca2+ (0.001-1 mM) potentiated the GABA stimulation of [35S]GTPgammaS binding in membranes prepared from CHO cells stably expressing the GABA(B)-R1/R2 **heterodimer**. The GABA EC50 was reduced from 72 to 7.7 microM by addition of 1 mM Ca2+, with no change in the maximum response. A similar effect was observed in membranes from rat brain cortex. Ca2+ also potentiated GABA inhibition of forskolin-stimulated cAMP levels in the CHO cells and enhanced coupling to GIRK K+ channels in Xenopus oocytes. Other divalent cations were ineffective. The effects of Ca2+ were found to be agonist dependent with baclofen having a reduced sensitivity compared to GABA. Calcium appears to act allosterically to enhance GABA responses at the GABA(B) receptor, however, unlike the Ca2+-sensing receptor and some of the mGluR family, Ca2+ does not act as a ligand in its own right.

L13 ANSWER 5 OF 6 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000069022 MEDLINE
DOCUMENT NUMBER: 20069022
TITLE: Functional pharmacology of cloned **heterodimeric** **GABAB** receptors expressed in mammalian cells.
AUTHOR: Brauner-Osborne H; Krogsgaard-Larsen P
CORPORATE SOURCE: NeuroScience PharmaBiotec Centre, Department of Medicinal Chemistry, The Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen, Denmark.. hans@medchem.dfh.dk
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (1999 Dec) 128 (7) 1370-4.
Journal code: B00. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY WEEK: 20000401
AB 1. In this study we report a new assay of **heterodimeric** gamma-amino-butanoic acid subtype B (**GABAB**) receptors where either **GABABR1a** or **GABABR1b** are co-expressed with **GABABR2** and the chimeric G-protein Galphaq-z5 in tsA cells. In this manner we obtained a robust response to **GABAB** agonists measured as increase in phosphoinositide hydrolysis. 2. We used this assay to characterize a number of commonly used **GABAB** receptor ligands. Both splice variants displayed the same rank order of agonist potency; 3-aminopropyl(methyl)phosphinic acid (SKF-97541)>GABA>(R)-4-amino-3-(4-chlorophenyl)butanoic acid ((R)-baclofen)>(RS)-4-amino-3-(5-chloro-2-thienyl)butanoic acid (BCTG)>3-aminopropylphosphonic acid (3-APPA) and furthermore, the absolute agonist potency values were very close to each

other. 3. 3-APPA wa[redacted] partial agonist displaying ma[redacted]al responses of 41 and 61% compared to [redacted]ABA at **GABABR1a** and **GABABR1b**, respectively. The antagonist (RS)-3-amino-2-(4-chlorophenyl)-2-hydroxypropylsulphonic acid (2-OH-saclofen) displayed KB values of 15 and 7.8 &mgr;M at **GABABR1a** and **GABABR1b**, respectively. 4. The rank order of agonist potency as well as the absolute ligand potencies correspond very well with those previously reported in different tissues, and this study thus provides a functional assay of cloned **GABAB** receptors which should be a valuable tool for further characterization of **GABAB** ligands. Finally, we can conclude that the functional pharmacological profiles of the two **GABABR1** splice variants are very similar.

L13 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:33120 BIOSIS
DOCUMENT NUMBER: PREV200000033120
TITLE: **GABAB** receptors - the first 7TM heterodimers.
AUTHOR(S): Marshall, Fiona H. (1); Jones, Kenneth A.; Kaupmann, Klemens; Bettler, Bernhard
CORPORATE SOURCE: (1) Receptor Systems, Molecular Pharmacology Unit, Glaxo Wellcome Medicines Research Centre, Gunnels Wood Road, Stevenage, SG1 2NY UK
SOURCE: Trends in Pharmacological Sciences, (Oct., 1999) Vol. 20, No. 10, pp. 396-399.
ISSN: 0165-6147.
DOCUMENT TYPE: Article
LANGUAGE: English

```
=> s heterodimer?

L14      26750 HETERODIMER?

=> d his

     (FILE 'HOME' ENTERED AT 16:10:24 ON 19 MAY 2000)

     FILE 'MEDLINE, BIOSIS, BIOTECHNO' ENTERED AT 16:10:41 ON 19 MAY 2000
L1         9581 S GABA? RECEPTOR
L2       536512 S HETERO?
L3          571 S L1 AND L2
L4          415 S L3 AND PY <1998
L5        10640 S COEXPRESSION
L6            8 S L4 AND L5
L7            7 DUP REM L6 (1 DUPLICATE REMOVED)
L8         3037 S GABAB
L9         3068 S GABAB?
L10         146 S L9 AND L2
L11       75555 S DIMER OR DIMERIC OR HETERODIMER OR HETERODIMERIC
L12           8 S L11 AND L9
L13           6 DUP REM L12 (2 DUPLICATES REMOVED)
L14       26750 S HETERODIMER?

=> s l14 and l9

L15          15 L14 AND L9

=> s l15 not l12

L16           7 L15 NOT L12

=> dup rem l16

PROCESSING COMPLETED FOR L16
L17           6 DUP REM L16 (1 DUPLICATE REMOVED)

=> d ibib abs 1-6
```

L17 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:484302 BIOSIS
DOCUMENT NUMBER: PREV199900484302
TITLE: **GABAB** receptors function as **heterodimers**
.
AUTHOR(S): Marshall, F. H. (1); White, J. (1); Main, M. (1); Green, A.
(1); Wise, A. (1)
CORPORATE SOURCE: (1) Receptor Systems, Molecular Pharmacology Unit, GlaxoWellcome Medicines Research Centre, Gunnels Wood Road,
Stevenage, Hertfordshire, SG1 2NY UK
SOURCE: Biochemical Society Transactions, (Aug., 1999) Vol. 27, No.
4, pp. 530-535.
Meeting Info.: 668th Meeting of the Biochemical Society Glasgow, Scotland, UK April 7-9, 1999 Biochemical Society
. ISSN: 0300-5127.
DOCUMENT TYPE: Conference
LANGUAGE: English

L17 ANSWER 2 OF 6 MEDLINE
ACCESSION NUMBER: 1999429981 MEDLINE
DOCUMENT NUMBER: 99429981
TITLE: **GABAB** receptors - the first 7TM **heterodimers**.
AUTHOR: Marshall F H; Jones K A; Kaupmann K; Bettler B
CORPORATE SOURCE: Receptor Systems, Molecular Pharmacology Unit, Glaxo Wellcome Medicines Research Centre, Gunnels Wood Road, Stevenage, UK SG1 2NY.. fhm27375@GlaxoWellcome.co.uk
SOURCE: TRENDS IN PHARMACOLOGICAL SCIENCES, (1999 Oct) 20 (10) 396-9. Ref: 26
Journal code: WFT. ISSN: 0165-6147.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
ENTRY MONTH: 200001
ENTRY WEEK: 20000104

L17 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:357020 BIOSIS
DOCUMENT NUMBER: PREV199900357020
TITLE: **Heterodimerisation** of **GABAB** receptors.
AUTHOR(S): Marshall, Fiona H. (1); White, Julia H. (1); Wise, Alan (1); Main, Martin J. (1); Green, Andrew (1); Fraser, Neil J. (1); Disney, Graham H. (1); Barnes, Ashley A. (1); Foord, Steven M. (1)
CORPORATE SOURCE: (1) Receptor Systems, Molecular Pharmacology Unit, Medicines Research Centre, Glaxo Wellcome, Gunnels Wood Road, Stevenage, Hertfordshire, SG1 2NY UK
SOURCE: Biochemical Society Transactions, (1999) Vol. 27, No. 3, pp. A70.
Meeting Info.: 668th Meeting of the Biochemical Society Glasgow, Scotland, UK April 7-9, 1999 Biochemical Society
. ISSN: 0300-5127.
DOCUMENT TYPE: Conference
LANGUAGE: English

L17 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:57890 BIOSIS
DOCUMENT NUMBER: PREV199900057890
TITLE: **GABAB**-receptor subtypes assemble into functional heteromeric complexes.
AUTHOR(S): Kaupmann, Klemens; Malitschek, Barbara; Schuler, Valerie; Heid, Jakob; Froestl, Wolfgang; Beck, Pascal; Mosbacher,

Joha[redacted]s; Bischoff, Serge; Kulik, Ako[redacted]Shigemoto, Ryuichi; Karschin, Andreas; Bettler, Bernhard (1)

CORPORATE SOURCE: (1) Novartis Pharma AG, TA Nervous Syst., CH-4002 Basel Switzerland

SOURCE: Nature (London), (Dec. 17, 1998) Vol. 396, No. 6712, pp. 683-687.
ISSN: 0028-0836.
DOCUMENT TYPE: Article
LANGUAGE: English

AB B-type receptors for the neurotransmitter GABA (gamma-aminobutyric acid) inhibit neuronal activity through G-protein-coupled second-messenger systems, which regulate the release of neurotransmitters and the activity of ion channels and adenylyl cyclase. Physiological and biochemical studies show that there are differences in drug efficiencies at different **GABAB** receptors, so it is expected that **GABAB**-receptor (**GABABR**) subtypes exist. Two **GABAB**-receptor splice variants have been cloned (**GABABR1a** and **GABABR1b**), but native **GABAB** receptors and recombinant receptors showed unexplained differences in agonist-binding potencies. Moreover, the activation of presumed effector ion channels in heterologous cells expressing the recombinant receptors proved difficult. Here we describe a new **GABAB** receptor subtype, **GABABR2**, which does not bind available **GABAB** antagonists with measurable potency. **GABABR1a**, **GABABR1b** and **GABABR2** alone do not activate Kir3-type potassium channels efficiently, but co-expression of these receptors yields a robust coupling to activation of Kir3 channels. We provide evidence for the assembly of heteromeric **GABAB** receptors in vivo and show that **GABABR2** and **GABABR1a**/b proteins immunoprecipitate and localize together at dendritic spines. The heteromeric receptor complexes exhibit a significant increase in agonist- and partial-agonist-binding potencies as compared with individual receptors and probably represent the predominant native **GABAB** receptor. Heteromeric assembly among G-protein-coupled receptors has not, to our knowledge, been described before.

L17 ANSWER 5 OF 6 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 1999087321 MEDLINE
DOCUMENT NUMBER: 99087321

TITLE: **Heterodimerization** is required for the formation of a functional GABA(B) receptor [see comments].

COMMENT: Comment in: Nature 1998 Dec 17;396(6712):629-30

AUTHOR: White J H; Wise A; Main M J; Green A; Fraser N J; Disney G H; Barnes A A; Emson P; Foord S M; Marshall F H

CORPORATE SOURCE: Receptor Systems, Molecular Pharmacology Unit, GlaxoWellcome, Medicines Research Centre, Stevenage, Hertfordshire, UK.

SOURCE: NATURE, (1998 Dec 17) 396 (6712) 679-82.
Journal code: NSC. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Cancer Journals; Priority Journals
OTHER SOURCE: GENBANK-AJ012185; GENBANK-AJ012186; GENBANK-AJ012188
ENTRY MONTH: 199903

AB GABA (gamma-aminobutyric acid) is the main inhibitory neurotransmitter in the mammalian central nervous system, where it exerts its effects through ionotropic (GABA(A/C)) receptors to produce fast synaptic inhibition and metabotropic (GABA(B)) receptors to produce slow, prolonged inhibitory signals. The gene encoding a GABA(B) receptor (GABA(B)R1) has been cloned; however, when expressed in mammalian cells this receptor is retained as an immature glycoprotein on intracellular membranes and exhibits low affinity for agonists compared with the endogenous receptor on brain membranes. Here we report the cloning of a complementary DNA encoding a new subtype of the **GABAB** receptor (GABA(B)R2), which we identified by mining expressed-sequence-tag databases. Yeast two-hybrid screening showed that

this new GABA(B)R2-[redacted]eptor subtype forms **heterodimer**[redacted]with GABA(B)R1 through an [redacted]nteraction at their intracellu[redacted] carboxy-terminal tails. Upon expression with GABA(B)R2 in HEK293T cells, GABA(B)R1 is terminally glycosylated and expressed at the cell surface. Co-expression of the two receptors produces a fully functional GABA(B) receptor at the cell surface; this receptor binds GABA with a high affinity equivalent to that of the endogenous brain receptor. These results indicate that, in vivo, functional brain GABA(B) receptors may be **heterodimers** composed of GABA(B)R1 and GABA(B)R2.

L17 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:57888 BIOSIS
DOCUMENT NUMBER: PREV199900057888
TITLE: **GABAB** receptors function as a heteromeric assembly of the subunits **GABABR1** and **GABABR2**.
AUTHOR(S): Jones, Kenneth A. (1); Borowsky, Beth; Tamm, Joe A.; Craig, Douglas A.; Durkin, Margaret M.; Dai, Meng; Yao, Wen-Jeng; Johnson, Mary; Gunwaldsen, Caryn; Huang, Ling-Yan; Tang, Cheng; Shen, Quanrong; Salon, John A.; Morse, Kelley; Laz, Thomas; Smith, Kelli E.; Nagarathnam, Dhanapalan; Noble, Stewart A.; Branchek, Theresa A.; Gerald, Christophe
CORPORATE SOURCE: (1) Synaptic Pharmaceutical Corp., 215 College Road, Paramus, NJ 07652 USA
SOURCE: Nature (London), (Dec. 17, 1998) Vol. 396, No. 6712, pp. 674-679.
ISSN: 0028-0836.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The principal inhibitory neurotransmitter GABA (gamma-aminobutyric acid) exerts its effects through two ligand-gated channels, GABAA and GABAC receptors, and a third receptor, **GABAB** (ref. 1), which acts through G proteins to regulate potassium and calcium channels. Cells heterologously expressing the cloned DNA encoding the **GABABR1** protein exhibit high-affinity antagonist-binding sites, but they produce little of the functional activity expected from studies of endogenous **GABAB** receptors in the brain. Here we describe a new member of the **GABAB** polypeptide family, **GABABR2**, that shows sequence homology to **GABABR1**. Neither **GABABR1** nor **GABABR2**, when expressed individually, activates GIRK-type potassium channels; however, the combination of **GABABR1** and **GABABR2** confers robust stimulation of channel activity. Both genes are co-expressed in individual neurons, and both proteins co-localize in transfected cells. Moreover, immunoprecipitation experiments indicate that the two polypeptides associate with each other, probably as **heterodimers**. Several G-protein-coupled receptors (GPCRs) exist as high-molecular-weight species, consistent with the formation of dimers by these receptors, but the relevance of these species for the functioning of GPCRs has not been established. We have now shown that co-expression of two GPCR structures, **GABABR1** and **GABABR2**, belonging to the same subfamily is essential for signal transduction by **GABAB** receptors.

=> s l9 and heteromer?

L18 16 L9 AND HETEROMER?

=> s l18 not l17

L19 14 L18 NOT L17

=> d his

(FILE 'HOME' ENTERED AT 16:10:24 ON 19 MAY 2000)

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      FILE 'MEDLINE, BIOSIS, BIOTECHNO' ENTERED AT 16:10:41 ON 19 MAY 2000
L1          9581 S GABA? RECEPTOR
L2        536512 S HETERO?
L3           571 S L1 AND L2
L4           415 S L3 AND PY <1998
L5         10640 S COEXPRESSION
L6             8 S L4 AND L5
L7             7 DUP REM L6 (1 DUPLICATE REMOVED)
L8          3037 S GABAB
L9          3068 S GABAB?
L10          146 S L9 AND L2
L11        75555 S DIMER OR DIMERIC OR HETERODIMER OR HETERODIMERIC
L12            8 S L11 AND L9
L13            6 DUP REM L12 (2 DUPLICATES REMOVED)
L14        26750 S HETERODIMER?
L15           15 S L14 AND L9
L16            7 S L15 NOT L12
L17            6 DUP REM L16 (1 DUPLICATE REMOVED)
L18           16 S L9 AND HETEROMER?
L19           14 S L18 NOT L17

=> s l19 not l12

L20           13 L19 NOT L12

=> dup rem l20

PROCESSING COMPLETED FOR L20
L21           10 DUP REM L20 (3 DUPLICATES REMOVED)

=> d ibib abs 1-10


L21  ANSWER 1 OF 10  BIOSIS  COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER:    2000:153416  BIOSIS
DOCUMENT NUMBER:     PREV200000153416
TITLE:               Ca2+ requirement for high-affinity gamma-aminobutyric acid
                     (GABA) binding at GABAB receptors: Involvement of
                     serine 269 of the GABABR1 subunit.
AUTHOR(S):           Galvez, Thierry (1); Urwyler, Stephan; Prezeau, Laurent;
                     Mosbacher, Johannes; Joly, Cecile; Malitschek, Barbara;
                     Heid, Jakob; Brabet, Isabelle; Froestl, Wolfgang; Bettler,
                     Bernhard; Kaupmann, Klemens; Pin, Jean-Philippe
CORPORATE SOURCE:    (1) Laboratoire des Mecanismes Moleculaires des
                     Communications Cellulaires, CCIPE-Centre National de la
                     Recherche Scientifique-UPR9023, 141 Rue de la Cardonille,
                     F-34094, Montpellier Cedex 5 France
SOURCE:              Molecular Pharmacology., (March, 2000) Vol. 57, No. 3, pp.
                     419-426.
                     ISSN: 0026-895X.
DOCUMENT TYPE:       Article
LANGUAGE:            English
SUMMARY LANGUAGE:    English
AB   The gamma-aminobutyric acid (GABA) receptor type B (GABABR) is
     constituted of at least two homologous proteins, GABABR1 and
     GABABR2. These proteins share sequence and structural similarity
     with metabotropic glutamate and Ca2+-sensing receptors, both of which are
     sensitive to Ca2+. Using rat brain membranes, we report here that the
     affinity of GABA and 3-aminopropylphosphinic acid for the GABABR
     receptor is decreased by a factor >10 in the absence of Ca2+. Such a
large
     effect of Ca2+ is not observed with baclofen or the antagonists CGP64213
     and CGP56999A. In contrast to baclofen, the potency of GABA in
stimulating
     GTPgammaS binding in rat brain membranes is also decreased by a factor
>10
     upon Ca2+ removal. The potency for Ca2+ in regulating GABA affinity was
37
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muM. In cells expre[redacted]ng **GABABR1**, the potency of GAB[redacted]but not of baclofen, in displacing bound 125I-CGP64213 was si[redacted]larly decreased in the absence of Ca2+. To identify residues that are responsible for the Ca2+ effect, the pharmacological profile and the Ca2+ sensitivity of a series of **GABABR1** mutants were examined. The mutation of Ser269 into Ala was found to decrease the affinity of GABA, but not of baclofen, and the GABA affinity was found not to be affected upon Ca2+ removal. Finally, the effect of Ca2+ on the **GABAB** receptor function is no longer observed in cells coexpressing this **GABABR1**-S269A mutant and the wild-type **GABABR2**. Taken together, these results show that Ser269, which is conserved in the **GABABR1** protein from Caenorhabditis elegans to mammals, is critical for the Ca2+-effect on the **heteromeric GABAB** receptor.

L21 ANSWER 2 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:196949 BIOSIS
DOCUMENT NUMBER: PREV200000196949
TITLE: Distribution of the **GABAB** receptor subunit gb2 in rat CNS.
AUTHOR(S): Clark, Janet A. (1); Mezey, Eva; Lam, Alan S.; Bonner, Tom I.
CORPORATE SOURCE: (1) Laboratory of Genetics, National Institute of Mental Health, 36 Convent Drive, Bethesda, MD, 20892-4094 USA
SOURCE: Brain Research, (March 31, 2000) Vol. 860, No. 1-2, pp. 41-52.
ISSN: 0006-8993.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have identified and isolated human and rat cDNAs for a novel receptor, gb2, with 38% homology to the **GABAB** receptors gb1a and gb1b. These receptors comprise a new subfamily of seven transmembrane G protein-coupled receptors (GPCRs) that share structure and sequence similarities with the metabotropic glutamate receptors. In situ hybridization histochemistry using an antisense probe to this novel receptor mRNA shows a distribution in rat CNS nearly identical to that for the gb1 receptor, although some regions showed significant differences. Specifically, message levels for gb2 were virtually absent in the caudate/putamen, and significantly lower in the medial basal hypothalamus, septum and brainstem as compared with gb1 message levels. In contrast to gb1, gb2 mRNA was never detected in white matter suggesting that gb2 message is found exclusively in neurons. Finally, in rat brain regions showing significant overlap of message for gb1 and gb2, the transcripts are often found in the same cells. Data from our previous work showing that coexpression of gb2 with gb1 is necessary for expression of a functional receptor together with the detailed anatomical data presented here indicate that native **GABAB** receptors function as **heteromeric** proteins, the most abundant form being the gb1/gb2 receptor. However, the more limited distribution of gb2 receptor mRNA suggests that there are brain regions where **GABAB** receptors are composed of gb1 and as yet unidentified family members.

L21 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:146861 BIOSIS
DOCUMENT NUMBER: PREV200000146861
TITLE: **Heteromeric GABAB** receptors are activated by gamma-hydroxybutyrate.
AUTHOR(S): Mosbacher, J. (1); Lingenhoehl, K. (1); Kaupmann, K. (1); Beck, P. (1); Pagano, A. (1); Brom, R. (1); Heid, J. (1); Ristig, D. (1); Meigel, I. (1); Schuler, V. (1); Klix, N. (1); Froestl, W. (1); Urwyler, S. (1); Bettler, B. (1)
CORPORATE SOURCE: (1) Neuroscience Research, Novartis Pharma AG, 4002, Basel Switzerland
SOURCE: Society for Neuroscience Abstracts., (1999) Vol. 25, No. 1-2, pp. 1480.
Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA October 23-28, 1999

Soci[redacted] for Neuroscience
. ISS[redacted] 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L21 ANSWER 4 OF 10 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000040717 MEDLINE
DOCUMENT NUMBER: 20040717
TITLE: G-protein-coupled inwardly rectifying potassium channels are targets of alcohol action.
AUTHOR: Lewohl J M; Wilson W R; Mayfield R D; Brozowski S J; Morrisett R A; Harris R A
CORPORATE SOURCE: Waggoner Center for Alcohol and Addiction Research and Section on Neurobiology, University of Texas at Austin, Austin, Texas 78712, USA.. lewohlj@mail.utexas.edu
CONTRACT NUMBER: AA06399 (NIAAA)
AA03527 (NIAAA)
GM47818 (NIGMS)
+
SOURCE: Nat Neurosci, (1999 Dec) 2 (12) 1084-90.
Journal code: DA8. ISSN: 1097-6256.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY WEEK: 20000304
AB G-protein-coupled inwardly rectifying potassium channels (GIRKs) are important for regulation of synaptic transmission and neuronal firing rates. Because of their key role in brain function, we asked if these potassium channels are targets of alcohol action. Ethanol enhanced function of cerebellar granule cell GIRKs coupled to **GABAB** receptors. Enhancement of GIRK function by ethanol was studied in detail using Xenopus oocytes expressing homomeric or **heteromeric** channels. Function of all GIRK channels was enhanced by intoxicating concentrations of ethanol, but other, related inwardly rectifying potassium channels were not affected. GIRK2/IRK1 chimeras and GIRK2 truncation mutants were used to identify a region of 43 amino acids in the carboxyl (C) terminus that is critical for the action of ethanol on these channels.

L21 ANSWER 5 OF 10 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:144595 BIOSIS
DOCUMENT NUMBER: PREV200000144595
TITLE: The **heteromeric GABAB** receptor recognizes G-protein alpha subunit C-termini.
AUTHOR(S): Blahos, Jaroslav (1); Franek, Miloslav; Pagano, Adriana; Kaupmann, Klemens; Bettler, Bernhard; Pin, Jean-Philippe
CORPORATE SOURCE: (1) CNRS UPR9023, Montpellier, 34094 France
SOURCE: Society for Neuroscience Abstracts., (1999) Vol. 25, No. 1-2, pp. 967.
Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA October 23-28, 1999
Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L21 ANSWER 6 OF 10 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999102694 MEDLINE
DOCUMENT NUMBER: 99102694
TITLE: Role of **heteromer** formation in **GABAB** receptor function [see comments].
COMMENT: Comment in: Science 1999 Jan 1;283(5398):14-5
AUTHOR: Kuner R; Kohr G; Grunewald S; Eisenhardt G; Bach A; Kornau

H C[redacted]
CORPORATE SOURCE: BAS[redacted]NX Bioscience AG, Department o[redacted]euroscience, Im Neuenheimer Feld 515, D-69120 Heidelberg, Germany.
SOURCE: SCIENCE, (1999 Jan 1) 283 (5398) 74-7.
Journal code: UJ7. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Cancer Journals; Priority Journals
OTHER SOURCE: GENBANK-AF109405
ENTRY MONTH: 199903

AB Recently, GBR1, a seven-transmembrane domain protein with high affinity for gamma-aminobutyric acid (GABA)B receptor antagonists, was identified. Here, a GBR1-related protein, GBR2, was shown to be coexpressed with GBR1 in many brain regions and to interact with it through a short domain in the carboxyl-terminal cytoplasmic tail. Heterologously expressed GBR2 mediated inhibition of adenylyl cyclase; however, inwardly rectifying potassium channels were activated by **GABAB** receptor agonists only upon coexpression with GBR1 and GBR2. Thus, the interaction of these receptors appears to be crucial for important physiological effects of GABA and provides a mechanism in receptor signaling pathways that involve a heterotrimeric GTP-binding protein.

L21 ANSWER 7 OF 10 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999061981 MEDLINE
DOCUMENT NUMBER: 99061981
TITLE: Human gamma-aminobutyric acid type B receptors are differentially expressed and regulate inwardly rectifying K+ channels.
AUTHOR: Kaupmann K; Schuler V; Mosbacher J; Bischoff S; Bittiger H;
Heid J; Froestl W; Leonhard S; Pfaff T; Karschin A; Bettler B
CORPORATE SOURCE: Novartis Pharma AG, TA Nervous System, CH-4002 Basel, Switzerland.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Dec 8) 95 (25) 14991-6.
Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-AJ225028; GENBANK-AJ225029
ENTRY MONTH: 199903

AB gamma-Aminobutyric acid type B receptors (**GABABRs**) are involved in the fine tuning of inhibitory synaptic transmission. Presynaptic **GABABRs** inhibit neurotransmitter release by down-regulating high-voltage activated Ca2+ channels, whereas postsynaptic **GABABRs** decrease neuronal excitability by activating a prominent inwardly rectifying K+ (Kir) conductance that underlies the late inhibitory postsynaptic potentials. Here we report the cloning and functional characterization of two human **GABABRs**, hGABABR1a (hR1a) and hGABABR1b (hR1b). These receptors closely match the pharmacological properties and molecular weights of the most abundant native **GABABRs**. We show that in transfected mammalian cells hR1a and hR1b can modulate **heteromeric** Kir3.1/3.2 and Kir3.1/3.4 channels. Heterologous expression therefore supports the notion that Kir3 channels are the postsynaptic effectors of **GABABRs**. Our data further demonstrate that in principle either of the cloned receptors could mediate inhibitory postsynaptic potentials. We find that in the cerebellum hR1a and hR1b transcripts are largely confined to granule and Purkinje cells, respectively. This finding supports a selective association of hR1b, and not hR1a, with postsynaptic Kir3 channels. The mapping of the **GABABR1** gene to human chromosome 6p21.3, in the vicinity of a susceptibility locus (EJM1) for idiopathic generalized epilepsies, identifies a candidate gene for inherited forms of epilepsy.

L21 ANSWER 8 OF 10 BIO[redacted] COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999[redacted]7862 BIOSIS
DOCUMENT NUMBER: PREV199900317862
TITLE: **Heteromerization** of **GABAB** receptors: A new principle for G protein-coupled receptors. (Satellite Symposium to the 28th Annual Meeting of the Society for Neuroscience) (Los Angeles, California, USA; November 5-7, 1998.
AUTHOR(S): Kaupmann, Jkenebs; Bettler, Bernard (1)
CORPORATE SOURCE: (1) TA Nervous System, Novartis Pharma AG, CH-4002, Basel Switzerland
SOURCE: CNS Drug Reviews, (Winter, 1998) Vol. 4, No. 4, pp. 376-379.
ISSN: 1080-563X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L21 ANSWER 9 OF 10 MEDLINE
ACCESSION NUMBER: 97338146 MEDLINE
DOCUMENT NUMBER: 97338146
TITLE: Activation of **heteromeric** G protein-gated inward rectifier K+ channels overexpressed by adenovirus gene transfer inhibits the excitability of hippocampal neurons [published erratum appears in Proc Natl Acad Sci U S A 1997
Aug 19;94(17):9511].
AUTHOR: Ehrengruber M U; Doupnik C A; Xu Y; Garvey J; Jasek M C; Lester H A; Davidson N
CORPORATE SOURCE: Division of Biology, 156-29, California Institute of Technology, Pasadena, CA 91125, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Jun 24) 94 (13) 7070-5.
Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Cancer Journals; Priority Journals
ENTRY MONTH: 199709
AB G protein-gated inward rectifier K+ channel subunits 1-4 (GIRK1-4) have been cloned from neuronal and atrial tissue and function as heterotetramers. To examine the inhibition of neuronal excitation by GIRKs, we overexpressed GIRKs in cultured hippocampal neurons from 18 day rat embryos, which normally lack or show low amounts of GIRK protein and currents. Adenoviral recombinants containing the cDNAs for GIRK1, GIRK2, GIRK4, and the serotonin 1A receptor were constructed. Typical GIRK currents could be activated by endogenous **GABAB**, serotonin 5-HT1A, and adenosine A1 receptors in neurons coinfected with GIRK1+2 or GIRK1+4. Under current clamp, GIRK activation increased the cell membrane conductance by 1- to 2-fold, hyperpolarized the cell by 11-14 mV, and inhibited action potential firing by increasing the threshold current for firing by 2- to 3-fold. These effects were not found in non- and mock-infected neurons, and were similar to the effects of muscarinic stimulation of native GIRK currents in atrial myocytes. Two inhibitory effects of GIRK activation, hyperpolarization and diminution of depolarizing pulses, were simulated from the experimental data. These inhibitory effects are physiologically important in the voltage range between the resting membrane potential and the potential where voltage-gated Na+ and K+ currents are activated; that is where GIRK currents are outward.

L21 ANSWER 10 OF 10 MEDLINE
ACCESSION NUMBER: 97040344 MEDLINE
DOCUMENT NUMBER: 97040344
TITLE: GABAc receptors: relatively simple transmitter -gated ion channels?.
AUTHOR: Johnston G A
CORPORATE SOURCE: Adrien Albert Laboratory of Medicinal Chemistry, Department
of Pharmacology, University of Sydney, NSW, Australia.

SOURCE: TREN[redacted]IN PHARMACOLOGICAL SCIENCES, 6 Sep) 17 (9)
319-[redacted] Ref: 30
Journal code: WFT. ISSN: 0165-6147.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
ENTRY MONTH: 199702
ENTRY WEEK: 19970204

AB The inhibitory neurotransmitter, GABA, activates a variety of receptors in all areas of the CNS. Two major subtypes of GABA receptors are well known: (1) GABAA receptors are ligand-gated Cl- channels that consist of a **heteromeric** mixture of protein subunits forming a pentameric structure, and (2) **GABAB** receptors couple to Ca2+ and K+ channels via G proteins and second messengers. Here, Graham Johnston discusses evidence for a third major subclass of GABA receptors. GABAC receptors appear to be relatively simple ligand-gated Cl- channels with a distinctive pharmacology, in that they are not blocked by bicuculline and not modulated by barbiturates, benzodiazepines or neuroactive steroids. Compared with GABAA receptors, GABAC receptors are activated at lower concentrations of GABA and are less liable to desensitization. In addition, their channels open for a longer time. The pharmacology of these novel subtypes of GABA receptors may yield important therapeutic agents.

=> d his

(FILE 'HOME' ENTERED AT 16:10:24 ON 19 MAY 2000)

FILE 'MEDLINE, BIOSIS, BIOTECHNO' ENTERED AT 16:10:41 ON 19 MAY 2000

L1	9581	S	GABA? RECEPTOR
L2	536512	S	HETERO?
L3	571	S	L1 AND L2
L4	415	S	L3 AND PY <1998
L5	10640	S	COEXPRESSION
L6	8	S	L4 AND L5
L7	7	DUP REM	L6 (1 DUPLICATE REMOVED)
L8	3037	S	GABAB
L9	3068	S	GABAB?
L10	146	S	L9 AND L2
L11	75555	S	DIMER OR DIMERIC OR HETERODIMER OR HETERODIMERIC
L12	8	S	L11 AND L9
L13	6	DUP REM	L12 (2 DUPLICATES REMOVED)
L14	26750	S	HETERODIMER?
L15	15	S	L14 AND L9
L16	7	S	L15 NOT L12
L17	6	DUP REM	L16 (1 DUPLICATE REMOVED)
L18	16	S	L9 AND HETEROMER?
L19	14	S	L18 NOT L17
L20	13	S	L19 NOT L12
L21	10	DUP REM	L20 (3 DUPLICATES REMOVED)

FILE 'HOME' ENTERED AT 14:04:44 ON 21 MAY 2000

=> file medline biosis biotechno

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'MEDLINE' ENTERED AT 14:05:02 ON 21 MAY 2000

FILE 'BIOSIS' ENTERED AT 14:05:02 ON 21 MAY 2000

FILE 'BIOTECHNO' ENTERED AT 14:05:02 ON 21 MAY 2000

=> s GABAB?

L1 3068 GABAB?

=> s gb2

L2 116 GB2

=> s l1 and l2

L3 4 L1 AND L2

=> dup rem l3

PROCESSING COMPLETED FOR L3
L4 3 DUP REM L3 (1 DUPLICATE REMOVED)

=> d ibib abs 1-3

L4 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:196949 BIOSIS
DOCUMENT NUMBER: PREV200000196949
TITLE: Distribution of the **GABAB** receptor subunit **gb2** in rat CNS.
AUTHOR(S): Clark, Janet A. (1); Mezey, Eva; Lam, Alan S.; Bonner, Tom I.
CORPORATE SOURCE: (1) Laboratory of Genetics, National Institute of Mental Health, 36 Convent Drive, Bethesda, MD, 20892-4094 USA
SOURCE: Brain Research, (March 31, 2000) Vol. 860, No. 1-2, pp. 41-52.
ISSN: 0006-8993.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have identified and isolated human and rat cDNAs for a novel receptor, **gb2**, with 38% homology to the **GABAB** receptors gb1a and gb1b. These receptors comprise a new subfamily of seven transmembrane G protein-coupled receptors (GPCRs) that share structure and sequence similarities with the metabotropic glutamate receptors. In situ hybridization histochemistry using an antisense probe to this novel receptor mRNA shows a distribution in rat CNS nearly identical to that for the gb1 receptor, although some regions showed significant differences. Specifically, message levels for **gb2** were virtually absent in the caudate/putamen, and significantly lower in the medial basal

hypothalamus, septum and brainstem as compared with gb1 message levels. In contrast to gb1, **gb2** mRNA was never detected in white matter suggesting that **gb2** message is found exclusively in neurons. Finally, in rat brain regions showing significant overlap of message for gb1 and **gb2**, the transcripts are often found in the same cells. Data from our previous work showing that coexpression of **gb2** with gb1 is necessary for expression of a functional receptor together with the detailed anatomical data presented here indicate that native **GABAB** receptors function as heteromeric proteins, the most abundant form being the gb1/**gb2** receptor. However, the more limited distribution of **gb2** receptor mRNA suggests that there are brain regions where **GABAB** receptors are composed of gb1 and as yet unidentified family members.

L4 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999175124 MEDLINE
DOCUMENT NUMBER: 99175124
TITLE: Identification of a **GABAB** receptor subunit, **gb2**, required for functional **GABAB** receptor activity.
AUTHOR: Ng G Y; Clark J; Coulombe N; Ethier N; Hebert T E; Sullivan R; Kargman S; Chateauneuf A; Tsukamoto N; McDonald T; Whiting P; Mezey E; Johnson M P; Liu Q; Kolakowski L F Jr; Evans J F; Bonner T I; O'Neill G P
CORPORATE SOURCE: Merck Frosst Center for Therapeutic Research, Kirkland, Quebec H9H 3L1, Canada.. gordon_ng@merck.com
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Mar 19) 274 (12) 7607-10.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-AF069755; GENBANK-AF056085; GENBANK-AF057085; GENBANK-AF095723; GENBANK-AF058795
ENTRY MONTH: 199906
ENTRY WEEK: 19990603
AB G protein-coupled receptors are commonly thought to bind their cognate ligands and elicit functional responses primarily as monomeric receptors. In studying the recombinant gamma-aminobutyric acid, type B (**GABAB**) receptor (gb1a) and a **GABAB**-like orphan receptor (**gb2**), we observed that both receptors are functionally inactive when expressed individually in multiple heterologous systems. Characterization of the tissue distribution of each of the receptors by in situ hybridization histochemistry in rat brain revealed co-localization of gb1 and **gb2** transcripts in many brain regions, suggesting the hypothesis that gb1 and **gb2** may interact in vivo. In three established functional systems (inwardly rectifying K+ channel currents in Xenopus oocytes, melanophore pigment aggregation, and direct cAMP measurements in HEK-293 cells), GABA mediated a functional response in cells coexpressing gb1a and **gb2** but not in cells expressing either receptor individually. This GABA activity could be blocked with the **GABAB** receptor antagonist CGP71872. In COS-7 cells coexpressing gb1a and **gb2** receptors, co-immunoprecipitation of gb1a and **gb2** receptors was demonstrated, indicating that gb1a and **gb2** act as subunits in the formation of a functional **GABAB** receptor.

L4 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:85564 BIOSIS
DOCUMENT NUMBER: PREV199900085564
TITLE: Functional expression and distribution of **GB2**, a second **GABAB** receptor.
AUTHOR(S): Clark, J. A.; Mezey, E.; Lam, A. S.; Bonner, T. I.
CORPORATE SOURCE: Sect. Genetics, NIMH, Bethesda, MD 20892-4094 USA

SOURCE: Society for Neuroscience Abstracts, (1998) Vol. 24, No. 1-2, pp. 1990.
Meeting Info.: 28th Annual Meeting of the Society for Neuroscience, Part 2 Los Angeles, California, USA November 7-12, 1998 Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English

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=> file medline biosis biotechno

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

FILE 'MEDLINE' ENTERED AT 16:10:41 ON 19 MAY 2000

FILE 'BIOSIS' ENTERED AT 16:10:41 ON 19 MAY 2000
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FILE 'BIOTECHNO' ENTERED AT 16:10:41 ON 19 MAY 2000
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=> s gaba? receptor

L1         9581 GABA? RECEPTOR

=> s hetero?

L2       536512 HETERO?

=> s l1 and l2

L3          571 L1 AND L2

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nested terms that are not separated by a logical operator.

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MISSING OPERATOR L3 PY<1998
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nested terms that are not separated by a logical operator.

=> s l1 py<1998

MISSING OPERATOR L1 PY<1998
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nested terms that are not separated by a logical operator.

=> s l1 py <1998

MISSING OPERATOR L1 PY
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nested terms that are not separated by a logical operator.

=> s l1 and py <1998
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SEARCH ENDED BY USER

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L4          415 L3 AND PY <1998

=> s coexpression
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WEST

Generate Collection

L14: Entry 3 of 3 File: DWPI Aug 12, 1999

DERWENT-ACC-NO: 1999-527300
DERWENT-WEEK: 199944

TITLE: New DNA encoding human and murine receptor subunits, useful for identifying agonists and antagonists for treatment of depression, epilepsy and neuropsychiatric disorders

INVENTOR: BONNER, T I; BONNERT, T P ; CLARK, J ; KOLAKOWSKI, L F ; LIU, Q ; MCDONALD, T ; NG, G Y K

PATENT-ASSIGNEE:

ASSIGNEE	CODE
MERCK & CO INC	MERI
MERCK FROSST CANADA INC	MERI
UNIV TEXAS HEALTH SCI CENT SAN ANTONI	UYTEN
US NAT INST OF HEALTH CENT SAN ANTONI	USSH

PRIORITY-DATA:
1998US-0073767 February 5, 1998

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9940114 A1	August 12, 1999	E	128	C07K014/705

DESIGNATED-STATES: CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION-DATA:

PUB-NO	APPL-DESCRIPTOR	APPL-NO	APPL-NO
WO 9940114A1	February 3, 1999	1999WO-US02361	N/A

INT-CL (IPC): C07K 14/705; C12N 5/10; C12N 15/09; C12N 15/11; C12N 15/12; C12N 15/62; G01N 33/566

ABSTRACTED-PUB-NO: WO 9940114A
BASIC-ABSTRACT:

NOVELTY - DNA encoding human and murine GABAB (metabotropic lambda -amino-butyric acid) receptor subunit proteins HG20 and GABABR1a respectively, are new.

DETAILED DESCRIPTION - HG20 has an amino acid sequence selected from amino acid 9, 35, 36, 38, 39, 42, 44, 46, 52 or 57 to amino acid 941 of a fully defined 941 amino acid sequence, and GABABR1a has a fully defined 960 amino acid sequence, both given in the specificati on.

INDEPENDENT CLAIMS are included for the following:

(1) isolated DNA (I) encoding HG20 comprising an amino acid sequence selected from residues 9-941, 35-941, 36-941, 38-941, 39-941, 42-941, 44-941, 46-941, 52-941 or 57-941 of the 941 amino acid sequence (I) given in the specification;

(2) an isolated DNA that hybridizes to HG20 DNA;

(3) an expression vector comprising HG20 DNA;

(4) a recombinant host cell comprising the vector;

(5) a protein (II) substantially free from other proteins, comprising HG20 having an amino acid sequence selected from residues 9-941, 35-941, 36-941, 38-941, 39-941, 42-941, 44-941, 46-941, 52-941 or 57-941 of (I) and optionally comprising a G-protein coupled receptor protein;

(6) a polypeptide (III) comprising a coiled-coil domain from the C-terminus of a GABAB receptor subunit and no other contiguous amino acid sequences longer than 5 amino acids from the same subunit, which mediates heterodimerization of the subunit with another GABAB receptor subunit;

(7) isolated DNA (IV) encoding GABABR1a having the sequence given in the specification;

(8) a protein, substantially free from other proteins, comprising a GABABR1a protein;

(9) identifying compounds (potential agonists or antagonists) which bind GABAB receptors, comprising:

(a) culturing recombinant cells containing vectors encoding HG20 and GABABR1a or GABABR1b;

(b) allowing the expressed HG20 to form heterodimers with expressed GABABR1a or GABABR1b;

(c) adding a labeled GABAB receptor ligand in the presence and absence of the test compound; and

(d) measuring the binding of the ligand to the heterodimers, where the compound is a potential agonist/antagonist when the amount of ligand binding is less in the presence of, than in the absence of the test compound;

(10) identifying HG20 agonists and antagonists, comprising:

(a) exposing cells containing expression vectors encoding HG20, and GABABR1a or GABABR1b, to a candidate GABAB receptor agonist; and

(b) measuring the functional response of the cells and comparing to controls;

(11) producing functional GABAB receptors in cells, comprising transfectin g with 2 expression vectors which express HG20, and GABABR1a or GABABR1b, allowing heterodimers between HG20 and GABABR1a or GABABR1b;

(12) an antibody specific to HG20;

(13) preparation of truncated HG20; and

(14) a chimeric HG20 protein having HG20 covalently linked at the N-terminus to non-HG20 amino acid sequence.

ACTIVITY - Antidepressant; anticonvulsant; nootropic; anxiolytics; antiasthmatic; relaxant.

MECHANISM OF ACTION - Inhibitors

USE - Cells expressing the new receptor subunits are useful for identifying GABAB receptor agonists and antagonists (claimed). HG20 proteins and their antagonists are useful for inhibiting HG20 or GABAB receptor function, useful for treating depression, epilepsy, neuropsychiatric disorders, dementias, muscular contractions, and CNS disorders. Agonists are useful for treating asthma, muscular contractions, epilepsy, neuropsychiatric disorders, dementias and muscle disorders.

CHOSEN-DRAWING: Dwg.0/27

TITLE-TERMS: NEW DNA ENCODE HUMAN MURINE RECEPTOR USEFUL IDENTIFY AGONIST ANTAGONIST TREAT DEPRESS EPILEPSY DISORDER

DERWENT-CLASS: B04 D16 S03

CPI-CODES: B04-E02D; B04-E03D; B04-E08; B04-F0100E; B04-F1100E; B04-G04; B04-K01K; B14-J01A1; B14-J01A4; B14-J05A; B14-J07; B14-K01A; B14-L01; B14-L06; B14-S03; D05-H08; D05-H09; D05-H11; D05-H12A; D05-H12E; D05-H14; D05-H17A4; D05-H17C;

EPI-CODES: S03-E14H4;

CHEMICAL-CODES:

Chemical Indexing M1 *01*
    Fragmentation Code
    M423 M710 M905 N135 P431 P444 P446 P517 P822 P831
    Q233
    Specfic Compounds
    A00NST A00NSN

Chemical Indexing M1 *02*
    Fragmentation Code
    M423 M710 M905 N135 P431 P444 P446 P517 P822 P831
    Q233
    Specfic Compounds
    A00GTT A00GTN

Chemical Indexing M1 *03*
    Fragmentation Code
    M423 M710 M905 N135 P431 P444 P446 P517 P822 P831
    Q233
    Specfic Compounds
    A00H3T A00H3N

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C1999-154834
Non-CPI Secondary Accession Numbers: N1999-390599

WEST

Generate Collection

L20: Entry 7 of 10 File: DWPI Oct 14, 1999

DERWENT-ACC-NO: 1999-610994
DERWENT-WEEK: 199952

TITLE: Novel nucleic acids, used to screen for specific modulators, e.g. for treating spasticity or Alzheimer's disease

INVENTOR: BUSBY, J G; GARRETT, J E ; SIMIN, R T ; STORMANN, T M

PATENT-ASSIGNEE:

ASSIGNEE	CODE
NPS PHARM INC	NPSPN

PRIORITY-DATA:
1998US-0080676 April 3, 1998

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9951636 A2	October 14, 1999	E	077	C07K014/47

DESIGNATED-STATES: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW

APPLICATION-DATA:

PUB-NO	APPL-DESCRIPTOR	APPL-NO	APPL-NO
WO 9951636A2	April 2, 1999	1999WO-US07352	N/A

INT-CL (IPC): A01K 67/027; C07K 14/47; C07K 16/28; C12N 5/06; C12N 15/12

ABSTRACTED-PUB-NO: WO 9951636A
BASIC-ABSTRACT:

NOVELTY - Purified nucleic acid (I) contains at least 18 contiguous nucleotides (nt) from a fully defined 2823 bp sequence given in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) expression vector containing (I);

(b) recombinant cells containing this vector;

(c) nucleic acid (Ia) of 20 nt, of which at least 18 are complementary to (I) or its perfect complement;

(d) purified polypeptides (II) containing at least 6 amino acids (aa) from a

fully defined 943 residue aa sequence given in the specification, representing the human gamma -aminobutyric acid receptor GABABR2;

(e) binding agent (III) specific for (II);

(f) recombinant production of (II), or its fragments, by culturing cells of (b);

(g) method for identifying modulators of (II) activity;

(h) co-expression system comprising, in a cell, at least one of GABABR1a or R1b, GABABR2 and Gq05;

(i) screening for compounds that act on GABABR1a, R1b or R2, using the system of (h); and

(j) transgenic non-human animals containing (I).

ACTIVITY - Antispastic; antineurodegeneration; analgesic; anti-addictive; cardiovascular.

MECHANISM OF ACTION - (II) modulate synaptic transmissions by inhibiting presynaptic transmitter release and by increasing potassium ion conductance (resulting in long-lasting inhibition of postsynaptic potentials).

USE - (I) are used

(1) for recombinant production of polypeptides (II), i.e. the human gamma -aminobutyric acid receptor GABABR2;

(2) as nucleic acid probes and primers for detecting (II)-encoding nucleic acid or similar sequences;

(3) to create transgenic animals;

(4) to identify antisense or related agents; and

(5) to express chimeric receptors.

(II) are used (i) to raise specific antibodies (Ab) and (ii) to identify specific modulators of GABABR2. These modulators are potentially useful for treating e.g. spasticity, motor control disorders, Alzheimer's or Huntington's diseases, pain, cognitive disorders, alcohol addiction (or withdrawal), feeding behavior, cardiovascular or respiratory disorders. Ab are used as therapeutic modulators; diagnostically for quantifying GABABR2, for affinity purification and for studying synthesis, structure and function of the receptor. Transgenic animals are useful for in vivo studies on the effects of GABABR2 and of agents that mimic or block this receptor.

CHOSEN-DRAWING: Dwg.0/4

TITLE-TERMS: NOVEL NUCLEIC ACID SCREEN SPECIFIC MODULATE TREAT SPASTICITY DISEASE

DERWENT-CLASS: B04 D16 P14

CPI-CODES: B04-C01; B04-E03D; B04-E05; B04-E06; B04-E08; B04-F0100E; B04-G04; B04-K01; B04-N04; B04-P0100E; B11-C08E; B12-K04E; B12-K04F; B14-C01; B14-F01; B14-F02; B14-J01A4; B14-J02; B14-J02B; B14-M01; B14-M01A; B14-M01C; D05-H08; D05-H09; D05-H12A; D05-H12E; D05-H14; D05-H16A; D05-H17A4;

CHEMICAL-CODES:

Chemical Indexing M1 *01*
    Fragmentation Code

M423 M710 M750 M781 M905 N102 P411 P446 P510 P520
P522 P625 P641 P642 P646 P820 P831 Q233 Q505
Specfic Compounds
A00H3T A00H3A A00H3D A00H3N

Chemical Indexing M1 *02*
Fragmentation Code
M423 M710 M750 M781 M905 N102 P411 P446 P510 P520
P522 P625 P641 P642 P646 P820 P831 Q233 Q505
Specfic Compounds
A00H1T A00H1A A00H1D A00H1N

Chemical Indexing M1 *03*
Fragmentation Code
M423 M710 M750 M781 M905 N102 P831 Q233 Q505
Specfic Compounds
A00NSA A00NSD A00NSN

Chemical Indexing M1 *04*
Fragmentation Code
M423 M710 M750 M781 M905 N102 P831 Q233 Q505
Specfic Compounds
A012PA A012PD A012PN

Chemical Indexing M1 *05*
Fragmentation Code
M423 M710 M905 P831 Q233
Specfic Compounds
A00GTN

Chemical Indexing M1 *06*
Fragmentation Code
M423 M710 M905 Q233
Specfic Compounds
A00C8N

Chemical Indexing M6 *07*
Fragmentation Code
M905 P411 P446 P510 P520 P522 P625 P820 P831 Q233
Q505 R515 R521 R627 R633 R637 R639

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C1999-177900
Non-CPI Secondary Accession Numbers: N1999-450204

WEST

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Term: gababr2

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Today's Date: 5/21/2000

DB Name	Query	Hit Count	Set Name
USPT,JPAB,EPAB,DWPI	gababr2	2	L21
USPT,JPAB,EPAB,DWPI	l18 same l12	10	L20
USPT,JPAB,EPAB,DWPI	l18 and l12	53	L19
USPT,JPAB,EPAB,DWPI	co-express$	1317	L18
USPT,JPAB,EPAB,DWPI	l16 same l12	8	L17
USPT,JPAB,EPAB,DWPI	dimer$	53491	L16
USPT,JPAB,EPAB,DWPI	gb2 same l13	0	L15
USPT,JPAB,EPAB,DWPI,TDBD	l12 same l13	3	L14
USPT,JPAB,EPAB,DWPI,TDBD	l2 or l4	2946	L13
USPT,JPAB,EPAB,DWPI,TDBD	GABA$	4344	L12
USPT,JPAB,EPAB,DWPI	l1 and l10	2	L11
USPT,JPAB,EPAB,DWPI	gb2	47050	L10
USPT	gababR$	0	L9
USPT	gababR2	0	L8
USPT	gabab	5	L7
USPT	gabab$	7	L6
USPT,JPAB,EPAB,DWPI,TDBD	s l4 and l1	0	L5
USPT,JPAB,EPAB,DWPI,TDBD	heterodimer$	2746	L4
USPT,JPAB,EPAB,DWPI,TDBD	l1 and l2	0	L3
USPT,JPAB,EPAB,DWPI,TDBD	heteromer$	275	L2
USPT,JPAB,EPAB,DWPI,TDBD	GABAB$	54	L1